## Remarks

Courtesies extended to Applicants' representative in telephone discussions of the above-referenced application on April 20, 2006, May 3, 2006, and May 26, 2006, are acknowledged with appreciation.

The present invention provides crystalline chalcone synthases and methods for crystallizing chalcone synthase and defined mutants thereof.

By the present communication, Claims 17, 40 and 43-45 have been amended to define Applicants' invention with greater particularity. No new matter is added as the amended claim language is fully supported by the specification and original claims. In view of the amendments submitted herewith, Claims 17, 23, 26, and 40-56 remain pending and under active consideration. The present status of all claims in the application, and current amendments thereto, is provided in the Listing of Claims presented herein beginning on page 2.

**Claim rejection under 35 U.S.C. § 112, first paragraph: Claims 17, 23, 26, and 40-56**

The rejection of Claims 17, 23, 26, and 40-56 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, is respectfully traversed.

Specifically, Applicants disagree with the Examiner's assertion that:

> The phrase "chalcone synthase having SEQ ID NO:1" expands the scope of the claims to include all possible protein crystals comprising the amino acid sequence of SEQ ID NO: 1 . . .

See page 2, lines 23-25 of the Office Action. Without acknowledging the merits of the Examiner's concerns, in an effort to expedite prosecution and reduce the issues (and consistent with the telephone conversations discussed above), independent Claims 17 and 40 have been

amended to replace the phrase "chalcone synthase having SEQ ID NO:1" with the phrase "chalcone synthase of SEQ ID NO:1."

Applicants further disagree with the Examiner's assertion that:

> . . . [(]claims 17, 23, 26, and 40-56[)] are directed to all possible crystals of protein comprising SEQ ID NO:1. The specification, however, only provides a single representative species of these crystals without any ligands . . .

See page 2, lines 25-27 of the Office Action (emphasis added). Contrary to the Examiner's assertion, the specification provides ample description of the species contemplated by the present claims (see MPEP § 2163). The Examiner's attention is drawn, for example, to numerous instances throughout the specification (e.g., Fig. 1B; Fig. 5A; page 148, Table 4; page 175, lines 19-21, page 176, line 29 to page 177, line 2; and page 177, lines 7-20) where crystalline forms of chalcone synthase with ligand are described, including crystalline complexes of chalcone synthase with representative ligands malonyl-CoA, hexanoyl-CoA, naringenin, and resveratrol.

Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

**Claim rejection under 35 U.S.C. § 112, first paragraph: Claims 17, 23, 26, and 40-56**

The rejection of Claims 17, 23, 26, and 40-56 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, is respectfully traversed.

Specifically, Applicants disagree with the Examiner's assertions that "[t]he crystallization condition at page 175, second paragraph, fails to identify the exact conditions, which the crystal can be grown" and that "[n]either the composition of the protein solution nor the final composition, in which the crystal is grown, is taught in the specification." (page 3, last two lines and page 4, lines 11-12 of the Office Action, respectively). Contrary to these mischaracterizations of the scope of the disclosure by the Examiner, the crystallization conditions described in the specification (page 175, paragraph 2) are submitted to be clear, reciting the

literal conditions of crystallization; i.e., vapor diffusion at a defined temperature (i.e., 4 degrees C) from a defined quantity of a defined solution (i.e., 2 μL drops of a 1:1 mixture of (1) 25 mg/mL protein and (2) crystallization buffer (2.2-2.4 M ammonium sulfate and 0.1 M PIPES, pH 6.5) in the presence or absence of 5 mM DTT (specification page 175, second paragraph)).

Fully consistent with the assertion that the crystallization conditions are fully enabled, the Examiner's attention is directed to the attached declaration of inventor Joseph P. Noel (i.e., the "Noel Declaration") under 37 C.F.R. § 1.132. In this declaration, the inventor confirms that protein employed for the crystallization described in the specification is provided as a solution containing 25 mg/ml protein in water prior to mixing with the defined crystallization buffer (see Item 5 of the Noel Declaration).

Applicants further disagree with the Examiner's assertion (Office Action , page 4, lines 12-13) that "[n]one of the buffer composition used in the purification and processing the protein is stated in the specification." Contrary to this mischaracterization of the scope of the disclosure, the specification at e.g., page 175, lines 3-13, provides clear instructions concerning purification and processing of the protein. Specifically, this passage discloses the subcloning, mutagenesis, expression, harvesting, and lysis of cells expressing chalcone synthase and mutants, all employing defined and readily understood methodologies. The specification (page 175, lines 9-13) further discloses post-processing (i.e., purification and His-tag removal) followed by additional chromatography steps, all employing defined and readily understood methodologies.

Applicants further disagree with the Examiner's assertion (Office Action, page 4, lines 13-14) regarding the alleged need for a "dialysis step to indicate that the protein was just in water." In contrast to the Examiner's assertion, the claims merely require crystallization of chalcone synthase (or mutant) from a defined solution, i.e., a defined concentration of protein in a 1:1 admixture with defined crystallization buffer. The Examiner's efforts to require a specific method (i.e., dialysis) for protein purification from among all methods available to one skilled in the art are misplaced. One of skill in the art would readily understand that a variety of techniques, e.g., dialysis, centrifugal concentration, desalting chromatography, and the like, could

be employed to obtain purified protein from which the required concentration of protein could be readily prepared for the practice of the crystallization method of the current invention.

Furthermore, Applicants respectfully disagree with the Examiner's assertion that "the phrase 'aqueous solution' does not mean that the protein is in unbuffered water solution free of any salts" (Office Action, page 4, lines 15-16). What the phrase means must be read in context. Specifically, the Examiner's attention is drawn to the specification at page 159, line 6 where the term "aqueous solution" is used to describe aqueous solutions of (previously grown) high-quality crystals which can be dissolved in water and then formulated to provide an aqueous solution having other uses. Thus, reference to the dissolution of the crystals of the invention in water at page 159, line 6 is fully consistent with the disclosure which contains no requirement for additional components, such as organic and inorganic salts, in the protein sample which is subject to crystallization after formation of a 1:1 admixture with a defined crystallization buffer. Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

**Conclusion**

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date September 29, 2006 By _____

FOLEY & LARDNER LLP
Customer Number: 30542
Telephone: (858) 847-6711
Facsimile: (858) 792-6773

Stephen E. Reiter
Attorney for Applicant
Registration No. 31,192